In re Application of: Michal DANIELY et al
Serial No.: 10/771,440
Filed: February 5, 2004
Office Action Mailing Date: June 10, 2009

Examiner: Bradley DUFFY
Group Art Unit: 1643
Attorney Docket: 26003

## REMARKS

Reconsideration of the above-identified Application in view of the amendments above and the remarks following is respectfully requested.

Claims 72, 73 and 82-86 are pending in this Application. Claims 72-73 and 82-86 have been rejected under 35 U.S.C. §112, second paragraph. Claims 72, 73, 82, 83 and 85 have been rejected under 35 U.S.C. §102(b). Claims 72, 73, 84 and 86 have been rejected under 35 U.S.C. §103(a). Claims 72, 73 and 82 have been amended herewith. New claims 87-92 have been added herewith.

The Application now comprises, after amendments, claims 72, 73 and 82-92, of which claims 72 and 73 are in independent form.

### ***Support For Claim Amendments***

Support for the amendments made in claims 72 and 73: " *which indicates that said single cell is* ***suspicious*** *as a transitional cell carcinoma cell*" [Page 27 (lines 15-18), Page 29 (lines 4-5) in the instant Application as filed]; *"wherein said chromosomal abnormality indicates that said cell is a transitional cell carcinoma cell"* [Page 2 (lines 31-33), Page 3 (lines 1-20) in the instant Application as filed]; *"wherein presence of said morphological abnormality and said chromosomal abnormality in the same said single cell* ***confirms*** *that said same single cell is a* ***transitional cell carcinoma*** *(TCC) cell"* [Page 28 (line 5), Page 28 (lines 30-33), Page 29 (lines 1-3) in the instant Application as filed].

Support for the amendments made in claim 82 can be found in Page 22 (lines 13-14); Page 23 (lines 8-13) in the instant Application as filed.

Support for New claims 87 and 88 can be found in Page 2 (lines 1-3); Page 7 (lines 29-31); Page 8 (lines 18-20); Page 28 (lines 16-17); Page 22 (line 7) in the instant Application as filed.

Support for New claims 89-90 can be found in Page 8 (lines 1-2) and Page 27 (lines 27-28) in the instant Application as filed.

Support for New claims 91-92 can be found in Page 27 (line 13) in the instant Application as filed.

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***35 U.S.C. §112 Rejections***

The Examiner has rejected claims 72-73 and 82-86 under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Specifically, the Examiner states that (a) the claims are indefinite in the recitation of "*identifying* a single cell having a *morphological abnormality associated with transitional cell carcinoma*" and "*identifying a chromosomal abnormality associated with said transitional cell carcinoma* in the same said single cell identified as having said *morphological abnormality associated with transitional cell carcinoma*"; that it is unclear how a morphological abnormality or a chromosomal abnormality is identified by these steps, for example, is it by May Grunwald-Giemsa, Giemsa, Papanicolau or Hematoxylin-Eosin? or in some other way?; and that it is unclear how these abnormalities are necessarily associated with transitional cell carcinoma; (b) the claims are indefinite because claim 72 is directed to a method of identifying transitional cell carcinoma cells and claim 73 is directed to a method of identifying bladder cancer, yet the claims merely recite processes which indicate that said same single cell is a cancerous cell, and the claims do not set forth that the presence of a "morphological" and "chromosomal" abnormality in the same cell indicates that the cell is a transitional cell carcinoma or indicates bladder cancer in the subject; The Examiner states that in the absence of a correlative step positively relating the whole of the process to its intended use, as recited in the preamble, the claim fails to delineate the subject matter that Applicant regards as the invention; (c) claim 82 is indefinite in the recitation of "wherein the transitional cell carcinoma cells are associated with bladder cancer or kidney cancer"; the Examiner states that without knowing the association between the transitional cell carcinoma cells and bladder cancer or kidney cancer the claims cannot be construed unambiguously. Examiner's rejections are respectfully traversed. Claims 72, 73 and 82 have been amended herewith. New claims 87-92 have been added herewith.

*Re: Item (a):*

While traversing Examiner's rejection and in order to expedite prosecution of this case, Applicants have amended claim 72 to recite *"identifying by said stain" in said images of step (b) a single cell having a morphological abnormality which*

*indicates that said single cell is suspicious as a transitional cell carcinoma (TCC) cell"*; and *"identifying by said FISH in said images of step (e) a chromosomal abnormality in the same said single cell identified in step (c) having said morphological abnormality, wherein said chromosomal abnormality indicates that said cell is a transitional cell carcinoma (TCC) cell"* (Emphasis added), to better clarify the claimed subject matter.

Claim 73 has been amended accordingly.

New dependent claims 87-92 pertaining to morphological or chromosomal abnormalities have been added.

*Re: Item (b):*

In order to expedite prosecution of this case, Applicants have amended claim 72 to recite *"wherein presence of said morphological abnormality and said chromosomal abnormality in the same said single cell indicates that said same single cell is a transitional cell carcinoma (TCC) cell"* (Emphasis added)

Accordingly, claim 73 has been amended to recite: *"wherein presence of said morphological abnormality and said chromosomal abnormality in the same said single cell indicates that said same single cell is a transitional cell carcinoma (TCC) cell; wherein said presence of said transitional cell carcinoma cell is indicative of a positive bladder cancer diagnosis"* (Emphasis added).

*Re: Item (c):*

In order to expedite prosecution of this case, Applicants have amended claim 82 to recite: *"wherein the transitional cell carcinoma cells are from a bladder cancer or a kidney cancer"* (Emphasis added).

In view of the above claim amendments and remarks Applicants believe to have overcome the 35 U.S.C. §112 rejections.

***35 U.S.C. §102 Rejections***

The Examiner has rejected claims 72, 73, 82, 83 and 85 under 35 U.S.C. §102(b) as being anticipated by Inoue et al. (Urol. Res. 28: 57-61, 2000).

Specifically, the Examiner states that Inoue et al., teach methods of identifying transitional cell carcinoma cells or diagnosing bladder cancer from a urine sample obtained via catheterization by a bladder washing of a subject, comprising:

(a) staining nucleated cells of the sample with Giemsa, Papanicolau to obtain stained nucleated cells;

(b) imaging said stained nucleated cells resultant of steps (a) so as to obtain images of said stained nucleated cells;

(c) identifying in said images of step (b) a single cell having a morphological abnormality stained by Giemsa of a transitional cell carcinoma, wherein the transitional cells were marked on the slides;

(d) staining said stained nucleated cells resultant of step (a) using FISH to thereby obtain stained nucleated cells stained with FISH, and subsequently,

(e) imaging said nucleated cells stained with FISH resultant of step (d) so as to obtain images of said nucleated cells stained with FISH, and subsequently; and

(f) identifying in said images of step (e) chromosome 9 monosome… in the same said single cell identified in step (c) having said morphological abnormality stained by Giemsa.

The Examiner states that because Inoue et al., teach methods of staining, imaging and identifying the same single cells from a urine sample as being transitional cells by Giemsa morphological staining and as having chromosome 9 monosomy, *i.e.,* a morphological abnormality of transitional cell carcinoma, the processes of Inoue et al. are deemed to be materially and manipulatively indistinguishable from the claimed process, and absent a showing of any difference, the processes disclosed by the prior art are deemed to anticipate the claimed processes. Examiner's rejection is respectfully traversed.

Applicants draws Examiner's attention that chromosome 9 monosomy is a chromosomal abnormality and not a morphological abnormality.

In addition, Applicants point out that the Examiner has mis-interpreted the art of Inoue et al. in stating that Inoue et al. identify a chromosomal abnormality (chromosome 9 monosomy) in the same said single cells identified in step (c) as having a morphological abnormality stained by Giemsa, since although Inoue et al., stained the exfoliated cells (from bladder washings at cystoscopy) by Giemsa in order

to identify clusters of transitional cells (Inoue Page 57, right column, 3rd paragraph), the identification of morphologically abnormal cells (such as class 5 cells) was performed on another sample of voided urine obtained before cystoscopy (Inoue Page 58, right column, lines 9-11) and not on the same exfoliated cells analyzed by FISH.

It should be noted that since exfoliated urine samples include clusters of cells (in which the boundaries between cells are not clear) Inoue T., et al. did not even attempt to perform cytology analysis on the exfoliated clusters stained by Giemsa. Moreover, the FISH analysis in Inoue was based on counting the number of signals in about 100 nuclei in the clusters regardless of their morphological characteristics (Inoue, Page 58, bridging paragraph), and not in a cell having a morphological abnormality which indicates that the cell is suspicious as a transitional cell carcinoma (TCC) cell as in the currently amended claimed invention.

Thus, one of ordinary skills in the art, when viewing the teachings of Inoue et al., could not have been motivated to identify transitional cell carcinoma cells from the Giemsa and FISH stained exfoliated cells of Inoue et al., since even Inoue et al. based their cytology analysis (which determines the presence or absence of morphologically abnormal cells) on another urine sample obtained from voided urine and not on the Giemsa-stained exfoliated cells which were analyzed by FISH.

In view of the above arguments and remarks Applicants believe to have overcome the 35 U.S.C. §102 (b) rejections.

***35 U.S.C. §103 Rejections***

*Inoue in view of U.S. Patent No. 6,418,236*

The Examiner has rejected claims 72, 73, 84 and 86 under 35 U.S.C. §103(a) as being unpatentable over Inoue et al., in view of U.S. Patent No. 6,418,236 (Ellis et al.). The Examiner states that while Inoue et al., teach methods of staining, imaging and identifying the same single cells from a urine sample as being transitional cells by Giemsa and as having chromosome 9 monosomy, *i.e.*, a morphological abnormality of transitional cell carcinoma that are materially and manipulatively indistinguishable from the claimed processes set forth in claims 72 and 73, Inoue et al does not expressly teach imaging the cells with an automated imaging device capable of dual

imaging, and that the deficiency is made up for in the teachings of U.S. Patent No. 6,418,236, which teaches automated image analysis using a microscope capable of dual imaging. The Examiner states that it would have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made to identify transitional cell carcinomas cells from a urine sample, by staining the cells by the processes of Inoue et al., and imaging the stained cells with the automated microscope capable of dual imaging taught by U.S. Patent No. 6,418,236 to identify the same single cells as transitional cell carcinoma cells. Examiner's rejection is respectfully traversed.

As indicated hereinabove, Applicants point that chromosome 9 monosomy is a chromosomal abnormality and not a morphological abnormality as was mistakenly indicated by Examiner.

Applicants point out that since as mentioned above, Inoue et al., describe analyzing two different urine samples, one for identification of a chromosomal abnormality in exfoliated cells stained by FISH and the other for identification of a morphological abnormality (e.g., identification of class 5 morphologically abnormal cells) in voided urine samples, and U.S. Patent No. 6,418,236 merely discloses a microscope capable of dual imaging, the combined art cannot be used to render the claimed invention obvious since none of them teach identifying the same single cell exhibiting a morphological abnormality and a chromosomal abnormality as in the claimed invention. Accordingly, the claimed invention is novel and inventive over the teachings of Inoue et al. and US Patent No. 6,418,236, either alone or in combination.

*Inoue in view of Kaplinsky (ASH meeting, 2001)*

The Examiner has rejected claims 72, 73, 84 and 86 under 35 U.S.C. §103(a) as being unpatentable over Inoue et al., in view of Kaplinsky (ASH meeting, 2001). The Examiner states that while Inoue et al., teach methods of staining, imaging and identifying the same single cells from a urine sample as being transitional cells by Giemsa and as having chromosome 9 monosomy, *i.e.*, a morphological abnormality of transitional cell carcinomas that are materially and manipulatively indistinguishable from the claimed processes set forth in claims 72 and 73, Inoue et al

does not expressly teach imaging the cells with an automated imaging device capable of dual imaging, and that the deficiency is made up for in the teachings of Kaplinsky, which teaches automated image analysis using a microscope capable of dual imaging to image the same cells stained with Giemsa and FISH. The Examiner states that it would have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made to identify transitional cell carcinoma cells from a urine sample, by staining the cells by the processes of Inoue et al., and imaging the stained cells with the automated microscope capable of dual imaging taught by Kaplinsky to identify the same single cells as transitional cell carcinoma cells. Examiner's rejection is respectfully traversed.

As indicated hereinabove, Applicants point that chromosome 9 monosomy is a chromosomal abnormality and not a morphological abnormality as was mistakenly indicated by Examiner.

Applicants point out that since as mentioned above, Inoue et al., describe analyzing two different urine samples, one for identification of a chromosomal abnormality in exfoliated cells stained by FISH and the other for identification of a morphological abnormality (e.g., identification of class 5 morphologically abnormal cells) in voided urine samples, and Kaplinsky merely discloses a microscope capable of dual imaging, the combined art cannot be used to render the claimed invention obvious since none of them teach identifying the same single cell exhibiting a morphological abnormality and a chromosomal abnormality as now claimed. Accordingly, the claimed invention is novel and inventive over the teachings of Inoue et al. and Kaplinsky, either alone or in combination.

In view of the above arguments and remarks Applicants believe to have overcome the 35 U.S.C. §103(a) rejections.

In view of the above amendments and remarks it is respectfully submitted that 72, 73 and 82-92 are now in condition for allowance. A prompt notice of allowance is respectfully and earnestly solicited.

Respectfully submitted,

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***Enclosures:***

- Additional Claims Transmittal Sheet; and
- Petition for Extension of Time (One Month)